I83G03 – 25 CAPSULES *ANNEX 3*

Pharmacia & Upjohn

Pharmaceutical Development / *Oral solids and warehousing*

PROCESSING SHEET

PAGE: 1 of *45*

PRODUCT: SU 10398 (PNU-290940AD) LOT: I83G03 COMM.: *RD000511POS ug*

PHARMACEUTICAL FORM: Capsule DOSAGE: 25 mg (as a free base)

FORMULA No.: 83HC02 PREPARATION DATE: *09/01*

PROCESSING START: *12/Sept./01* PROCESSING FINISH: *04/Oct./01*

THEORETICAL QUANTITY: 140000 qs (T) QUANTITY OBTAINED: *125 987* yield: *89.3* %

SCOPE OF THE PREPARATION: Stability studies and clinical trial

THEORETICAL UNITARY FORMULA

RAW MATERIAL		SPECIFICATIONS	M.U.	UNIT DOSE	Over Dose
SU10398 (PNU-29090AD)	Active principle		*mg*	*33.400* ①	
Mannitol	Excipient compensation	*NF*	*mg*	*39.663*	
Croscarmellose sodium			*mg*	*5.010*	
Povidone K25			*mg*	*4.175*	
Vegetable Magnesium Stearate			*mg*	*1.252*	
total			*mg*	*83.500*	
SHELLS, Format 3, Swedish orange opaque hard gelatin head/body			*mg*	*49 ± 4*	
① Equal to 25 mg as free base					

Signature of who filled out the form:

[signature]

Approval for use by the Chief of ORAL SOLIDS and WAREHOUSING:

[signature]

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: 2 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

PRACTICAL FORMULATION

RAW MATERIALS	CODE	LOT No.	TITER	Over dose	M.U.	PRACTICAL UNIT DOSE	M.U.	Practical quantity per 140000
SU10358 (PNU-290430AD)	*1502*	[illegible]	*99.666 (A)*	—	*mg*	*33.512*	*g*	*4631.670 (B)*
Mannitol NF	*723*	*AE 130*			*mg*	*39.551*	*g*	*5537.150 (B)*
Croscarmellose sodium	*718*	*AE 112*			*mg*	*2.505*	*g*	*350.700 (B)*
Povidone K25	*931563000*	*AA10G041*			*mg*	*4.175*	*g*	*584.500 (B)*
Total granulate					*mg*	*79.743*	*g*	*11164.020*
Croscarmellose sodium	*718*	*AE 112*			*mg*	*2.505*	*g*	*350.700*
Vegetable Magnesium Stearate	*927406000*	*AA10L028*			*mg*	*1.252*	*g*	*175.280*
Total					*mg*	*83.500*	*g*	*11690.000*
~~*SHELLS Format 3 White opaque hard gelatin Head/Body*~~								
SHELLS Format 3 Swedish orange opaque hard gelatin Head/Body	*1491*	*AE310*					*N*	*150.000**
**ordered in excess to compensate for losses in phases of processing* [initials] *12/09/01*								

NOTE: *(B) Equal to 74.6% as free base B*

(B) Total Quantity – During processing these are subdivided into two loads of Granulate. B

Operator's signature: [signature]

Verifier's signature: [signature]

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: 3 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

ACTIVE PRINCIPLE: VERIFICATION OF THE PRACTICAL QUANTITY CALCULATIONS AND AVERAGE TITER

Active principle: _____ Provided quantity: _____ **A)**

Lot: _____ Titer as sampled: _____

Active principle: _____ Provided quantity: _____ **B)**

Lot: _____ Titer as sampled: _____

Active principle: _____ Provided quantity: _____ **C)**

Lot: _____ Titer as sampled: _____

NOT APPLICABLE [initials] *12/09/01*

Total theoretical quantity	(Pt)	=	_____ g	(Unit dose x theoretical launch quantity)
Calculated theoretical quantity	(Pc)	=	_____ g	(A x Tit. A + B x Tit. B + C x Tit. C)
Total practical quantity	(Pp)	=	_____ g	(A + B + C)

NOTE:
1) The correspondence between the weighed active principle quantity and the practical active principle to be used is verified when **Pt = Pc.**
This correspondence is also verified when the two values differ and the divergence between the provided quantity and the requested quantity is due exclusively to the weighted values in accordance with the divergence limits set out in procedure SF.TF 015/0 **(±0.5%).**
2) If the condition in point 1) is not fulfilled, suspend the processing and inform the Lot Formation Center.
3) If the condition in point 1) is fulfilled, proceed to fill in the following points on this page.

Average titer weight = Pt/Pp x 100 = _____ %

Active principle: _____

Quantity to use = Pt/Titer* x 100 = _____ g **(D)**

Compensation excipient: _____

Quantity to use = Pe – (D – Pt) = _____ g

NOTE:
Pt = Weight in grams of the active principle considering a 100% titer
Pe = Compensation excipients weight in function of the active principle at 100% titer
* = Should multiple lots be used, the titer will be the average weight, as calculated considering the quantity of each lot.

Operator's signature: _____ **Verifier's signature:** _____

Checked by: _____

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: 4 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

CLEANING OF THE EQUIPMENT AND ROOMS

Once the processing has been completed clean the processing rooms with: *See Cleaning method 50/cm019*

Once the processing has been completed, clean the equipment with: *See Cleaning method 50/cm019*

PROCESSING IDENTIFICATION LABELS

CONFORMITY VERIFICATION LABELS		DATE:	*12/09/2001*	SIGNATURE:	[signature]
LABELS DELIVERED	No.: *32*	DATE:	*17/09/2001*	SIGNATURE:	[signature]
ADDITIONAL DELIVERED	No.:	DATE:	/ /	SIGNATURE:	
LABELS USED	No.: *30*	DATE:	*04/10/2001*	SIGNATURE:	[signature]
DETERIORATED LABELS	No.:	DATE:	/ /	SIGNATURE:	
LABELS RETURNED	No.: *2*	DATE:	*04/10/2001*	SIGNATURE:	[signature]

(The returned labels are destroyed)

LABEL MODEL

Pharmacia & Upjohn – *Oral Solids Section*
Product: SU10398 (PNU-290940AD) Capsule 25 mg (as a free base)
LOT: I83G03 Prep. Date: 09/2001
FORMULA No.:83HC02
.....
Date: *12/09/2001* Label No. 16 of 16
[signature]

Pharmacia & Upjohn – *Oral Solids Section*

SU10398 (PNU-290940AD)

Capsule 25 mg (as a free base)

LOT: I83G03 Prep. Date: 09/2001

FORMULA No.: 83HC02

Gross:..... **Tare**..... **Net:**.....

Date: *12/09/2001* Label No. 16 of 16
[signature]

NOTE

Pharmacia & Upjohn

Pharmaceutical Development / *Oral solids and warehousing*

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: 5 of 45

Room: 72

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WEIGHT VERIFICATION OF THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 ~~*02*~~ [init] *09* *17*	1 1/1	~~**Check the weight of the active principle/s**~~ *In accordance with the indications of the procedural deviation num. 31/01, weigh out the quantity of active principle indicated below.* [initials] *12/09/01* PRODUCT: *SU 10398 (PNU-29090AD)* LOT: *(D1) 6106-TJF-0101-N1* PRACTICAL WEIGHT *2345.835* g	Lot: *(B1) 6106-TSF-0101-N1* Gross: *2562* g Tare: *215* g Net: *2347* g Scale ID No.: *80-BL-35*	[initials]	[initials]
01 *09* *18*	1/2	PRODUCT: *SU 10398 (PNU-290940AD)* LOT: *(B1) 6106-TJF-0101-N1* PRACTICAL WEIGHT *2345.835* g	Lot: *(B1) 6106-TSF-0101-N1* Gross: *2561* g Tare: *215* g Net: *2346* g Scale ID No.: *80-BL-35*	[initials]	[initials]
	1/3	PRODUCT: LOT: PRACTICAL WEIGHT g	Lot: Gross: g Tare: g Net: g Scale ID No.: [initials] *12/09/2001*		

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Pharmaceutical Development / *Oral solids and warehousing*

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: *6* of *45*

Pharmaceutical form: Capsule Room: *72* Dosage: 25 mg (as a free base)

WEIGHT VERIFICATION OF THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 17	2	**Check the weight of the following raw materials:** *relative to the 1st load of granulate* [initials] *12/09/01*			
	2/1	PRODUCT: *Mannitol NF*	Lot: *AE130*		
			Gross: *2800.0* g		
		LOT: *AE 130*	Tare: *30.0* g	[initials]	[initials]
		PRACTICAL WEIGHT *2768.575* g	Net: *2720.0* g		
			Scale ID No.: *SO-BL-35*		
	2/2	PRODUCT: *Croscarmellose sodium*	Lot: *AE112*		
			Gross: *188.10* g		
		LOT: *AE112*	Tare: *13.00* g	[initials]	[initials]
		PRACTICAL WEIGHT *175.350* g	Net: *175.10* g		
			Scale ID No.: *SO-BL-35*		
	2/3	PRODUCT: *Povidone K25*	Lot: *AA1060A1*		
			Gross: *306.00* g		
		LOT: *AA10G041*	Tare: *13.00* g	[initials]	[initials]
		PRACTICAL WEIGHT *292.250* g	Net: *293.00* g		
			Scale ID No.: *SO-B2-35*		
	2/4	PRODUCT:	Lot:		
			Gross: g		
		LOT:	Tare: g		
		PRACTICAL WEIGHT g	Net: g		
		[initials] *12/09/01*	Scale ID No.:		
	2/5	PRODUCT:	Lot:		
			Gross: g		
		LOT:	Tare: g		
		PRACTICAL WEIGHT g	Net: g		
			Scale ID No.:		

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72 Page: 7 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 17	3	**Preparation of the granulated solution**			
	3/1	Using a sterile container, collect approximately 150 mL of contrast T.D.I. Water to be used and send the sample to determine its bacterial load.	T.D.I. Water Contrast No.: 42 mL collected: 150	[initials]	[initials]
	3/2	Weigh out 875 g of TDI H_2O Warm the solvent to a temperature between ____°C and ____°C and disperse under shaking: Let it cool until a practically clear solution is obtained.	Solvent Quantity Gross: 1020 g Tare: 145 g Net: 825 g Temperature: TA °C	[initials]	[initials]
	-	Addition of tensioactive agents ☐ Weight ____g of ____ Warm the solvent to a temperature between ____°C and ____°C and disperse under shaking: Combine the tensioactive solution with the solution of point ____ under shaking. [initials] 12/09 2001	Solvent Quantity per Tensioactive Gross: ____g Tare: ____g Net: ____g Temperature: ____°C [initials] 12/09 2001 ☐		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72 Page: 8 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01	4	**Preliminary sieve analysis of the raw materials**			
09 17	4/1-	Sieve analyze the raw materials *Mannitol NF* *Croscarmellose sodium* *Povidone K25* through a *1-1.5 mm* gauge sieve - Equipment type: *sieve*	Equipment used: *SIEVE* ID number: — Cleaning verification: — Gauge: *1 mm*	[initials]	[initials]
01 09 17	5	**Mixing** Load the raw materials from point *1/1and4/1* into the Diosna granulator and mix for *5* minutes under the following conditions: Principle shaker speed: *1* Crusher speed: *1* *Modify the operating conditions if necessary* [initials] *12/09/01*	ID number: *SO-QU-04* Cleaning verification: *OK* Principle shaker speed: *1* Crusher speed: *1* Start time: *14:16* End time: *14:21*	[initials]	[initials]
01 09 17	6 6	**Wetting** Wet the powder with the solution prepared in point *3* Using a peristaltic pump ☒ *Modify the operating conditions if necessary* [initials] *12/09/01* Pump capacity *250/350* g/min. During the wetting employ the following conditions: Principle shaker speed: *1* Crusher speed: *1*	Peristaltic pump model: ID number: *SO-QU-07* Cleaning verification: *OK* Pump capacity *240-260* g/min. Pump r.p.m. *40-42* Principle shaker speed: *1* Crusher speed: *1* Start time: *14:45* End time: *14:49*	[initials]	[initials]

Pharmacia & Upjohn

Pilot Plan Formula Development

Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *9* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**WET GRANULATION in DIOSNA**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 *09* *17*	*6/2*	If needed, add ..*T.D.I. H_2O*.. at the end of the wetting ~~while keeping the conditions from point ..6/1.. unchanged~~. *Setting the most appropriate conditions. Record each added* [illegible] *of H2O* [init] *12/09/01*	Solvent type: ..*T.D.I. H_2O*.. Added quantity: ..*416 g*.. T.D.I. Water contrast No.: ..*42*.. Start time: ..*15:05*.. End time: ..*15:07*..	[initials]	[initials]
	6/3	If the T.D.I. Water contrast is different from that in point ..*3*.., using a sterile container, collect approximately ..*150*.. ml of T.D.I. Water and send the sample to have its bacteria load determined.	T.D.I. Water contrast No.: .. mL collected: .. *17-09-01* [initials]		
01 *09* *17*	*7* *7/1*	**Granulation** Proceed to the granulation of the wet mass according to the following parameters: Principle shaker speed: ..*I/II*.. Crusher speed: ..*I/II*.. * Granulation time: ..*At least one minute*.. **Set the condition and times so that a consolidated granulate.* [initials] *12/09/01*	*Start time: 15:14* Principle shaker speed: ..*II*.. Crusher speed: ..*II*.. Principle motor electricity absorption at the end of granulation: ..*3.50*.. A Granulation time: ..*1'50"*.. *End time: 15:16*	[initials]	[initials]

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DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
	8	**Drying**			
01 09 17	8/1	Transfer the wet granulated mass into the ..... GLATT GPCG5 ..... type dryer and dry at a relative humidity of ≤ 2.5 % according to the following parameters:	Equipment: GLATT GPCG5 ..... ID number: SO-LF-02 ..... Cleaning verification: OK	[initials]	[initials]
	-	**Heater** ☐			
		Temperature: ..... °C			
		In a vacuum at ..... ☐	Temperature read: ..... °C		
		At an atmospheric pressure of ☐	Degree of vacuum:		
			Start time: ..... End time:		
	-	**Fluid bed dryer** ☒	[initials] 12/09 2001		
01 09 17	8a [illegible] 12 9 01	"AIR IN" Temperature: 60 °C	"AIR IN" Temperature: 60 °C	[initials]	[initials]
		"AIR IN" Volume: * Nm^3/h	"AIR IN" Volume: from 300 to 150 Nm^3/h		
	-	Product temperature to set on the thermometric probe: 40 °C	Temperature set on the probe: 40 °C		
		Time for shaking the hoses: ~15"	Time for shaking the hoses: 15"		
		Time between hose shakings: 3 minutes	Time between hose shakings: 3 minutes		
	-	Shaking Type WSG ☐	Shaking Type WSG ☐		
	-	GPCG ☒	GPCG ☒	[initials]	[initials]
	-				
		**Set the air volume so as to obtain the correct movement of the product.* [initials] 12/09/01	Start time: 15:38 End time: 16:01 "AIR OUT" Temperature at the end of the process: 32 °C		

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Pilot Plan Formula Development

Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *22/69*	Page: *11* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**WET GRANULATION in DIOSNA**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	*8/3*	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks:			[initials]
	8/4	Karl Fischer: ☐ *until a constant weight is achieved.* [initials] *12/09/01*	Residual humidity: : *1.29* %	[initials]	
	8/5	Weight loss at *110* °C ~~for ..... min.~~ ☒	Thermobalance at *110* °C ~~for~~ *P.C.* ~~min~~		
	8/6	Residual humidity limit ≤ *2.5* %	Thermobalance ID number: *SO-BL-42*		
			Karl Fischer ID number: –		
	8/7	If the residual humidity value is not within the set limits, continue drying according to the provisions in point *8/21*	☐		
	8/8	If necessary modify:	[initials] *18-09-01*		
		-the drying temperature ☐	"AIR IN" Temperature: ..... °C		
			Heater temperature: ..... °C		
	8/9	-the thermometric probe product temperature ☒	Thermometric probe product temperature: ..... °C		
			Start time: ..... End time:		
			"AIR OUT" temperature at the end of the process: ..... °C		
	8/10	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks again:			
			[initials] *8/10/01*		
	8/11	Karl Fisher: ☐	Residual humidity: : ..... %		
	8/12	*until a constant weight is achieved.* [initials] *12/09/01*	Thermobalance at ..... °C for ..... min		
	8/13	Weight loss at ..... °C ~~for ..... min.~~ ☒	Thermobalance ID number:		
		Residual humidity limit ≤ *2.5* %	Karl Fischer ID number:		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *12* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	9	**Final Calibration**			
	9/1	Calibrate the dried granulated mass using *OSCILLATING VIANI* that is equipped with a sieve with a gauge of *1000* µm	Equipment used: *OSCILLATING VIANI* ID number: *80-95-03* Cleaning verification: *OK* Gauge: *1000* µm Start time: *9:00* End time: *9:20*	[initials]	[initials]
18 Sept. 01	9/2	At the end of calibration, collect the granulated mass obtained in the appropriate container/s of *DOUBLE PE BAG INSERTED into a kraft barrel*	☒	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72-69 Page: 13 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base) **Granulation completion**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 09 01	10	**Technological controls**			
	10/1	Sample 50 g of granulate according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: 50 g Equipment: STAV 2003		
	10/2	Apparent density (SOP SF.TF 036) ☐ Limit of: NOT PLANNED g/mL	Quantity of mix used: 50 g V_0: 24 mL V_{10}: 70 mL V_{500}: 52 mL V_{1250}: 52 mL V_{2500}: – mL Da = 0.626 g/mL Di = 0.961 g/mL	[initials]	[initials]
18 Sept. 01	10/3	Granulometry (SOP SF.TF 034) ☐ Limits NOT PLANNED > 1000 µm: CP 12/09/01 % between 710 and 1000 µm: % between 500 and 710 µm: % between 250 and 500 µm: % between 106 and 250 µm: % < 106 µm: %	Equipment: [illegible] 200 Quantity of mix used: 50 g > 1000 µm: ~~10.0~~ % between 710 and 1000 µm: 10 % between 500 and 710 µm: 15 % between 250 and 500 µm: 17 % between 106 and 250 µm: 37 % < 106 µm: 21 %	[initials]	[initials]
	-	**Analytic controls**			
	-	Collect ____ (number of) granulated samples (in duplicate), according to SOP SF.CF 004 and send them to analysis for homogeneity control.	[initials] 12/09/01 Quantity sampled: ____ g See analytical controls in process		
18 09 01	11	**Granulation yield control**	**Granulation obtained:**		
	11/1	Determine the net quantity of granulated mass obtained from the sampling for technological and analytical controls.	Gross: 8495 g Tare: 3175 g Net: 5320 g ~~(D)~~	[initials]	[initials]
	11/2	~~Granulation yield % = D / theoretical~~	~~GRANULATION YIELD % = ____ (E)~~ B 17/09/01		

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Pharmaceutical Development / *Oral solids and warehousing*

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: *14* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)I Room: *72*

WEIGHT VERIFICATION OF THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	*12*	**Check the weight of the following raw materials:**			
18 Sept. 01	*12/1*	PRODUCT: *Mannitol NF* LOT: *AE130* PRACTICAL WEIGHT *2768.575* g	Lot: *AE130* Gross: *2799* g Tare: *30* g Net: *2769* g Scale ID No.: *SO-BL-35*	[initials]	[initials]
18 Sept. 01	*12/2*	PRODUCT: *CROSCARMELLOSE SODIUM* LOT: *AE112* PRACTICAL WEIGHT *175.350* g	Lot: *AE 112* Gross: *189* g Tare: *13* g Net: [illegible] g Scale ID No.: *SO-BL-35*	[initials]	[initials]
	12/3	PRODUCT: *POVIDONE K25* LOT: *AA10G041* PRACTICAL WEIGHT *292.250* g	Lot: *AA10G04* Gross: *305.3* g Tare: *13.0* g Net: *292.3* g Scale ID No.: *SO-BL-32*	[initials]	[initials]
		PRODUCT: LOT: PRACTICAL WEIGHT g	Lot: Gross: g Tare: g Net: g Scale ID No.:		
		PRODUCT: LOT: PRACTICAL WEIGHT g	Lot: Gross: g Tare: g Net: g Scale ID No.:		

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *15* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**WET GRANULATION in DIOSNA**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
	13	**Preparation of the granulated solution**			
	13/1	*If the contrast is different from the one in point 3 B 12/09/2001* Using a sterile container, collect approximately *150* mL of contrast T.D.I. water to be used and send the sample to determine its bacterial load.	T.D.I. Water Contrast No.: — mL collected: —		[initials]
	13/2	Weigh out *875* g of *T.D.I. H_2O*	Solvent Quantity Gross: *1020* g Tare: *145* g Net: *825* g Temperature: *TA* °C		
18-Sept. 01		Warm the solvent to a temperature between ..... °C and ..... °C and disperse under shaking: Let it cool until a practically clear solution is obtained.		[initials]	
		Addition of tensioactive agents ☐ Weight ..... g of ..... Warm the solvent to a temperature between ..... °C and ..... °C and disperse under shaking: Combine the tensioactive solution with the solution of point ..... under shaking.	Solvent Quantity per Tensioactive Gross: ..... g Tare: ..... g Net: ..... g Temperature: ..... °C *B 12/03/01* ☐		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *16* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18-Sept. 01	*14*	**Preliminary sieve analysis of the raw materials**			
	14/1	Sieve analyze the raw materials *Mannitol NF* *Croscarmellose Sodium* *Povidone* through a *1-1.5 mm* gauge sieve	Equipment used: *SIEVE* ID number: *I* Cleaning verification: *OK* Gauge: [illegible]	[initials]	[initials]
	14/2	Equipment type: *sieve*			
18-Sept. 01	*15*	**Mixing** Load the raw materials from point *½ and 14* into the Diosna granulator and mix for *5* minutes under the following conditions: Principle shaker speed: *I* Crusher speed: *I* *Modify the operating conditions if necessary B 12/09/2001*	ID No.: *80-GU-04* Cleaning verification: *–* Principle shaker speed: *I* Crusher speed: *I* Start time: *10:00* End time: *10:05*	[initials]	[initials]
18-Sept. 01	*16* *16/1*	**Wetting** Wet the powder with the solution prepared in point *13* Using a peristaltic pump ☒ *Modify the operating conditions if necessary B 12/09/2001* Pump capacity *250/350* g/min. During the wetting employ the following conditions: Principle shaker speed: *I* Crusher speed: *I*	Peristaltic pump model: *LOHER* ID No.: *80-PM-07* Cleaning verification: *–* Pump capacity *240-260* g/min. Pump r.p.m. *40-42* Principle shaker speed: *I* Crusher speed: *I* Start time: *10:25* End time: *10:30*	[initials]	[initials]

Pharmacia & Upjohn

Pilot Plan Formula Development

Oral Solids Section

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *17* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	*16/2*	If needed, add ..*TDI H_2O*.. at the end of the wetting ~~while keeping the conditions from point ..... unchanged.~~ *Setting the appropriate conditions. Record each addition of H_2O* [initials] *12/09/01*	Solvent type: ..*TDI H_2O*.. Added quantity: ..*450 S*.. T.D.I. Water contrast No.: ..*42*.. Start time: ..*10:40*.. End time: ..*10:43*..	[initials]	[initials]
	16/3	If the T.D.I. Water contrast is different from that in point ..*13*.., using a sterile container, collect approximately ..*50*.. ml of T.D.I. Water and send the sample to have its bacteria load determined.	T.D.I. Water contrast No.: ..–.. mL collected: ..–..		
18 Sept. 01	*17*	**Granulation**	*START TIME: 10:49*	[initials]	[initials]
	17/1	Proceed to the granulation of the wet mass according to the following parameters: Principle shaker speed: ..*I/II*.. Crusher speed: ..*I/II*.. Granulation time: ..[illegible] *1 min.*.. **Set the condition and times so that a consolidated granulate.* [initials] *12/09/01*	Principle shaker speed: ..*II*.. Crusher speed: ..*II*.. Principle motor electricity absorption at the end of granulation: ..*2.50*.. A Granulation time: ..*1'*.. *END TIME 10:50*		

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Pilot Plan Formula Development

Oral Solids Section

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72 Page: 18 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base) **WET GRANULATION in DIOSNA**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	18	**Drying**			
	18/1	Transfer the wet granulated mass into the ..... GLAT GPCG 5 ..... type dryer and dry at a relative humidity of ≤ 3.5 % according to the following parameters:	Equipment: ..... GLAT GPCG 5 ..... ID number: ..... 80-LF-02 ..... Cleaning verification: ..... OK	[initials]	[initials]
	-	**Heater**			
		Temperature: ..... °C			
		In a vacuum at ..... ☐	Temperature read: ..... °C		
		At an atmospheric pressure of ☐	Degree of vacuum:		
			Start time: ..... End time:		
	18/2	**Fluid bed dryer** ☒	[initials] 12/09/01		
18 Sept. 01		"AIR IN" Temperature: ..... 60 ..... °C	"AIR IN" Temperature: ..... 60 ..... °C		
		"AIR IN" Volume: ..... * ..... Nm^3/h	"AIR IN" Volume: ..... DA300A 150 ..... Nm^3/h	[initials]	
	-	Product temperature to set on the thermometric probe: ..... 40 ..... °C	Temperature set on the probe: ..... 40 ..... °C		[initials]
	-	Time for shaking the hoses: ..... ~15 sec	Time for shaking the hoses: ..... 15"		
	-	Time between hose shakings: ..... 3 ..... minutes	Time between hose shakings: ..... 3 ..... minutes		
	-	Shaking Type WSG ☐ GPCG ☒	Shaking type WSG ☐ GPCG ☒		
18 Sept. 01		**Set the air volume so as to obtain the correct movement of the product* [initials] 12/09/01	Start time: ..... 11:10 ..... End time: 11:38		
			"AIR OUT" Temperature at the end of the process: ..... 32 ..... °C	[initials]	
					[initials]

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72-69* Page: *19* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	*18/3-*	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks:			
	18/4	Karl Fisher: ☐ *until a constant weight is obtained* [initials] *12/03/01*	Residual humidity: *1.97* %	[initials]	[initials]
	18/5	Weight loss at *110* °C ~~for ..... min.~~ ☒	Thermobalance at *110* °C ~~for~~ *P.C.* ~~min~~		
	18/6	Residual humidity limit ≤ *2.5* %	Thermobalance ID number: *80-BE-42*		
			Karl Fischer ID number: –		
	18/7	If the residual humidity value is not within the set limits, continue drying according to the provisions in point *18/2 /*	☐		
	18/8	If necessary modify:			
		-the drying temperature ☐	"AIR IN" Temperature: ..... °C		
			Heater temperature: ..... °C		
	18/9	-the thermometric probe product temperature ☒	Thermometric probe product temperature: ..... °C		
			Start time: ..... End time:		
			"AIR OUT" temperature at the end of the process: ..... °C		
	18/10	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks again:	[initials] *08/10/01*		
	18/11	Karl Fisher: ☐ *until a constant weight is obtained* [initials] *12/03/01*	Residual humidity: ..... %		
	18/12	Weight loss at *110* °C ~~for ..... min.~~ ☒	Thermobalance at ..... °C for ..... min		
	18/13	Residual humidity limit ≤ *2.5* %	Thermobalance ID number:		
			Karl Fischer ID number:		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *20* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

WET GRANULATION in DIOSNA

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	*19*	**Final Calibration**			
	19/1	Calibrate the dried granulated mass using *OSCILLATING VIANI*	Equipment used: *OSCILLATING VIANI*		[initials]
		that is equipped with a sieve with a gauge of *1000* µm	ID number: *80-G8-03* Cleaning verification: – Gauge: *1000* µm Start time: *11:00* End time: *11:30*	[initials]	
18 Sept. 01	*19/2*	At the end of calibration, collect the granulated mass obtained in the appropriate container/s of *DOUBLE PE BAG INSERTED INTO A KRAFT BARREL*	☒	[initials]	[initials]

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72/69 Page: 21 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

Granulation completion

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	20	**Technological controls**			
	20/1	Sample 50 g of granulate according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: 50 g Equipment: STAV 2003		[initials]
	20/2	Apparent density (SOP SF.TF 036) ☒ Limit of: NOT PLANNED g/mL	Quantity of mix used: 50 g V_0: 78 mL V_{10}: 70 mL V_{500}: 64 mL V_{1250}: 64 mL V_{2500}: – mL Da = 0.641 g/mL Di = 0.281 g/mL	[initials]	
18 Sept. 01	20/3	Granulometry (SOP SF.TF 034) ☒ Limits NOT PLANNED [initials] 12/09/01 > 1000 µm: %	Equipment: JEL 200 Quantity of mix used: 50 g > 1000 µm: 0 %		[initials]
		between 710 and 1000 µm: %	between 710 and 1000 µm: 1 %		
		between 500 and 710 µm: %	between 500 and 710 µm: 9 %		
		between 250 and 500 µm: %	between 250 and 500 µm: 9 %	[initials]	
		between 106 and 250 µm: %	between 106 and 250 µm: 34 %		
		≤ 106 µm: %	< 106 µm: 52 %		
	-	~~Analytic controls~~			
	-	Collect ... (number of) granulated samples (in duplicate), according to SOP SF.CF 004 and send them to analysis for homogeneity control.	[initials] 12/09/01 Quantity sampled: ... g See analytical controls in process		
18.09.01	21	**Granulation yield control** *Combine: granulate from point 19/2 and 11*	**Granulation obtained:**		
	21/1	Determine the net quantity of granulated mass obtained from the sampling for technological and analytical controls:	Gross: 8624 g Tare: 3133 g Net: 5491 g **(D)**		
	21/2	Granulation yield % = D / theoretical / 100 *Theoretical = 11164.020 g* [initials] 12/09/01	GRANULATION YIELD % = 96.8 **(E)** *TOTAL 10811 g * (SEE NOTE)*		

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Pharmaceutical Development / *Oral solids and warehousing*

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *22* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base) **Granulation completion**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	22-	**Mix preparation**			
	22/1	Redo the proportions and weigh the excipients listed below based on the granulation yield (**E**) calculated in point *21/2* Send the residual excipients to be destroyed.	☒ *START TIME: 15:30*		
	22/2	*Croscarmellose sodium*	Lot: *AE112*		
18 Sept. 01		Quantity to be weighed = *350.700* g x E/100 = *339.578 g*	Gross: *952.5* g Tare: *13.0* g Net: *339.5* g	[initials]	[initials]
		Lot: *AE112*	Scale ID number: *SO-136-37*		
		Veg. Mg. STEARATE	Lot: *AA10L028*		
	22/3	Quantity to be weighed = *175.280* g x E/100 = *169.671 g*	Gross: *102.2* g Tare: *13.0* g Net: *169.7* g	[initials]	[initials]
		Lot: *AA10L028*	Scale ID number: *S0-BL-31* *END TIME: 16:05*		
	-		Lot:		
		Quantity to be weighed = ... g x E/100 = ...	Gross: ..... g Tare: ..... g		
		Lot:	Net: ..... g Scale ID number:		
	-		Lot:		
		Quantity to be weighed = ... g x E/100 = ...	Gross: ..... g Tare: ..... g		
		Lot:	Net: ..... g Scale ID number:		
	-		Lot:		
		Quantity to be weighed = ... g x E/100 = ...	Gross: ..... g Tare: ..... g [initials] *12/09/01*		
		Lot:	Net: ..... g Scale ID number:		

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *03/3* Page: *23* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base) **Granulation completion**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
	23	**Preliminary sieve analysis of the raw materials**	[initials] *19-09-01*		
	23/1	Sieve analyze the raw materials:	Equipment used: ~~*TURBULA T-50-A*~~		
		Croscarmellose sodium	*SIEVE*		
01		*Vegetable Mg. Stearate*	ID number: ~~*SO-145-23*~~		
09			Cleaning verification: *OK*		
19			Gauge: *0.365 mm*	[initials]	
		through a *0.365*			[initials]
		gauge sieve.			
	23/2	Equipment type: *sieve*			
	24	**Mixing**			
	24/1	Load the granulate from point *21* and the raw	Equipment used:		
01		materials that fulfill the provisions of point *23*,	*TURBULA*		
09		with the exception of *Mg. STEARATE*,	ID number: *SO-MS-23*		
19		into the *Turbula T50/A*	Cleaning verification: *OK*		
		50 L Barrel type mixer and mix for *5*	r.p.m.: *25*		
		minutes at a speed of *25* rpm.	Start time: *9:45* End time: *9:50*	[initials]	[initials]
	24/2	Add *Mg. STEARATE* to	Start time: *9:55* End time: *10:00*		
		the premix described in point *24/1* and mix	r.p.m.: *25*		
		for *5* minutes at a speed of *25* rpm.			
	24/3	At the end of mixing, empty the mix into the			
		appropriate container of	☒		
		~~*Double PE bag/Kraft Barrel*~~ [initials] *12/09/01*			
		50 L STEEL BARREL			

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Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 72/69 Page: 24 of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

Granulation completion

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 19	25	***Technological controls***			
	25/1	Sample ~55 g of mix according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: 55 g		
	25/2	Apparent density (SOP SF.TF 036) ☒ *SU 50 g* Limit of: NOT g/mL *PLANNED* [initials] 12/09 2001	Equipment: STAV 2003 Quantity of mix used: 50 g V_0: 68 mL V_{10}: 62 mL V_{500}: 58 mL V_{1250}: 58 mL V_{2500}: – mL Da = 0.735 g/mL Di = 0.862 g/mL *L.O.D. = 1.60%*		
	25/3	*Run a L.O.D. check at 110°C until a constant weight is achieved* [initials] *12/09/01*			
	~~25/3~~	Granulometry (SOP SF.TF 034) ☐ Limits > 1000 µm: ..... % between 710 and 1000 µm: ..... % between 500 and 710 µm: ..... % between 250 and 500 µm: ..... % between 106 and 250 µm: ..... % < 106 µm: ..... %	Equipment: ..... Quantity of mix used: ..... g > 1000 µm: ..... % between 710 and 1000 µm: ..... % between 500 and 710 µm: ..... % between 250 and 500 µm: ..... % between 106 and 250 µm: ..... % < 106 µm: *B 12-03/2001* ..... %	[initials]	[initials]
01 09 19	25/4-	**Analytic controls**			
	25/5	Collect 10 (number of) mix samples (in duplicate), according to SOP SF.CF 004 and send them to analysis for homogeneity control:	*SINGLE SAMPLES OF 150 mg EACH* Quantity sampled: L g [initials] *08/10/01* See analytical controls in process	[initials]	[initials]
01 09 19	26-	**Final mix yield control**	**Mix obtained:**		
	26/1	Determine the net quantity of mix obtained from the sampling for technological and analytical controls.	Gross: 11436 g Tare: 168 g Net: 11268 g	[initials]	[initials]

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *25* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

DISTRIBUTION into CAPSULES

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
20 - 09 - 01	*27*	**Distribution into capsules**			
	27/1	Verify the conformity of the hard gelatin shells: Format No.: *3* Body: *OPAQUE SWEDISH ORANGE* Head: *OPAQUE SWEDISH ORANGE* Printing: *–* *LOT No. AE310*	Conforms: Yes ☒ No ☐ *LOT No. AE310*	[initials]	[initials]
	27/2-	Weigh 100 empty shells to determine the average weight.	Average shell weight: *48* mg (α)		
	27/3	Make the *[illegible] A25* type capsule sealing machine ready and set it to format No. *3* with No. *2* dosage dispensing. *format 4*	Capsule sealing machine: *[illegible] A25* ID number: *SO-OP-05* Cleaning verification: *OK* Dispenser No.: *2* Format No.: *4*	[initials]	[initials]
20 -Sept - 01	*27/4*	Work Parameters Theoretical weight: *83.5* mg Distribution weight: Theoretical + α Weight limit: β + (± *7.5* % of the theoretical)	Distribution weight: *131.50* mg (β) Top end weight: *137.76* mg Bottom end weight: *125.24* mg	[initials]	[initials]
20 - Sept - 01		Hopper level height: *TBD* mm Dispenser chamber height: *TBD* mm	Hopper level: *30* mm Dispenser chamber: *10.5* mm		
	27/5	Piston pressure Yes ☐ No ☒	Pressure index: *–*	[initials]	[initials]
	27/6	Teflon coated pistons Yes ☐ No ☒	Yes ☐ No ☒		
	27/7	Machine speed: *~3500* cps/h	Machine speed: *3500* cps/h Production speed: *3500* cps/h	[initials]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *26* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		DISTRIBUTION into CAPSULES

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
20 Sept. 01	*27/8*	During the distribution, guide the produced capsules into a cyclone separator.	Model: *[illegible]* ID number: *SO-SL-01* Cleaning verification: *OK* Operative parameters: *35%* *SEE NOTE*	[initials]	[initials]
	27/9	As they come out of the cyclone, collect the capsules in suitable container/s of: *DOUBLE PE BAG / KRAFT BARREL*	Container used: * *20/09/01* *DOUBLE PE BAG / KRAFT BARREL*	[initials]	[initials]
20 - 09 - 01	*28*	**Sampling and controls**			
	28/1	Monitor the processing so that the process is executed within the set parameters and perform the following controls according to the manner indicated in SOP SF.CF 004 and the indications shown on the corresponding section of the form.		[initials]	[initials]
20 - 09 - 01	*29*	**Preparations for the sampling of the finished product for controls**			
	29/1	At the beginning, middle and end of the distribution into capsules, sample (in a manner equally spread throughout) an overall number of capsules equal to *~600* units which are necessary for controls on the finished product.	☒	[initials]	[initials]
20-Sept. 01	*30*	**DISTRIBUTION START**	Date: *20-Sept-01* Time: *16:00*	[initials]	[initials]

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72* Page: *27* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

DISTRIBUTION into CAPSULES

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
20 Sept. 01	*31*	**Controls while in process**			
	31/1	Capsule appearance at the beginning of distribution (that there are no signs of rupture or crushing on the body and/or tips)	Capsule appearance at the beginning of distribution *CONFORMS*	[initials]	[initials]
	31/2	Uniformity of weight/average weight (SOP SF.CI 051)	☒		
	31/3	Disintegration (SOP SF.CI 015)	☒		
	-	Uniformity of contents ☐ (sample 30 capsules at the beginning – middle – end of distribution and send the samples to SF/Pharmaceutical Controls)	Beginning ☐ Middle ☐ End ☒ [initials] *13/09/01*		
20 09 01	*31/4*	Capsule appearance at the end of distribution (that there are no signs of rupture or crushing on the body and/or tips)	Capsule appearance at the end of distribution *CONFORMS*	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *28* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)

Scale model: *SARTORIUS* ID number: *SO - BL - 37*

Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations
Start/End of processing/day and every *30 min*	*131.50 mg*	*137.76 mg*	*125.24 mg*	*20*	*31/2*

DATE	TIME	SINGLE WEIGHT VALUES										AVG	S.D.	CV%
20 Sep 01	*16:00*											*131.9*	*30*	*1.52*
	16:30	[illegible]										*131*	*1.6*	*1.22*
	17:00											*131.7*	*1.1*	*0.89*
21 Sept 01	*09:30*											*131.1*	*0.9*	*0.69*
	10:00											*130.3*	*0.8*	*0.61*
	10:30											*131.3*	*1.3*	*0.99*
	11:00											*131*	*1.3*	*0.99*
	11:30											*131.1*	*1.1*	*0.84*
	12:00											*131.7*	*1.3*	*0.99*
24 Sep 01	*09:10*											*130.7*	*1.1*	*0.84*
	09:40											*132.9*	*1.4*	*1.05*
	10:10											*133*	*1.5*	*1.13*
	10:40											*132.6*	*1.8*	*1.37*
	11:10								*M*	*D.S.*	*CV%*	*132.0*	*1.1*	*1.29*
	11:40	*MACHINE TIME STOPPED. RESTARTED 11:58 (SEE* [illegible]*)*							*131.8*	*1.3*	*0.99*	~~*130.1*~~	~~*5.1*~~	~~*4.38*~~
	13:30											*132.8*	*1.2*	*0.90*
	14:00											*133.2*	*1.4*	*1.05*
	14:30											*132.8*	*1.5*	*1.13*
	15:00											*133.0*	*1.6*	*1.20*
	15:30											*133.1*	*1.1*	*0.83*
	16:00											*133.1*	*1.7*	*1.28*
	16:30											*132.7*	*1.6*	*1.21*
25-09-01	*9:30*											*130.1*	*2.0*	*1.53*
	10:00											*131.5*	*1.8*	*1.37*
	10:30											*133.3*	*2.0*	*1.50*
MACHINE STOPPED							*25-09-01* [initials]							
START [illegible] *25/09/01*	*13:15*	*STOP*												

24.9.2001 [signature

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

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Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		DISTRIBUTION into CAPSULES

IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)

Scale model: *SARTORIUS* ID number: *SO - BL - 37*

Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations
Start/End of processing/day and every *30 min*	*131.50 mg*	*137.76 mg*	*125.24 mg*	*20*	*31/2*

DATE	TIME	SINGLE WEIGHT VALUES	AVG	S.D.	CV%
25-03-2001	*13:30*		*131.9*	*1.3*	*0.99*
	14:00		*131.8*	*1.1*	*1.29*
STOP	*14:30*		*132.6*	*1.6*	*1.21*
26-9-01	*10:15*	*M D.S. CV%*	*131.7*	*1.3*	*0.99*
STOP	*10:45*	*132.0 1.5 1.19*	~~*131.1*~~	~~*3.2*~~	~~*2.44*~~
	11:30	*RESTART AFTER BRIEF STOP OF THE MACHINE* [initials] *26/04/01*	*132.2*	*1.8*	*1.36*
STOP	*12:00*		*131.3*	*1.6*	*1.23*
26/9/01	*13:30*	*MACHINE ADJUSTMENT AND STOP* [initials] *21/09/01 TIME 14:59*	*131.1*	*1.5*	*1.14*
26/9/01	*16:20*	*RESTART AFTER STOP FOR ADJUSTMENT* [initials] *26/09/01*	*130.8*	*0.8*	*0.61*
26/9-01	*16:50*		*131.3*	*1.8*	*1.37*
27-09-01	*08:30*		*130.5*	*3.1* ~~*3.6*~~	*1.58*
	09:00		*131.3*	*1.2*	*0.91*
	09:30		*133.1*	*1.1*	*1.28*
	10:00	*MACHINE STOP* [initials] *27/09/01*	*132.4*	*1.9*	*1.66*
	11:00		*132.7*	*1.3*	*0.98*
	11:30		*134.3*	*1.3*	*0.97*
	12:00		*133.3*	*1.2*	*0.90*
	12:30		*133.3*	*1.8*	*1.35*
	13:00		*132.2*	*1.6*	*1.21*
	13:30		*133*	*1.7*	*1.28*
	14:00		*133.6*	*1.8*	*1.35*
	14:30		*133.9*	*1.9*	*1.05*
	15:00		*131.5*	*1.4*	*1.06*
	15:30		*132.5*	*1.3*	*0.98*
	16:00	*MACHINE STOP* *21 May 01* [signature]			
	16:15		*132.1*	*1.4*	*1.06*
27-SEP-01	*16:45*		*132.1*	*1.4*	*1.06*
28-09-2001	*08:10*		*131.7*	*1.9*	*1.44*

26-09-200
[signature

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Pharmacia & Upjohn

Pharmaceutical Development / *Oral Solids and Warehousing*

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 30 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		DISTRIBUTION into CAPSULES

IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)

** SEE NOTES 01/10/01*

Scale model: *SARTORIUS* ID number: *SO - BL - 37/31*

Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations
Start/End of processing/day and every *30 min*	*131.50 mg*	*137.76 mg*	*125.24 mg*	*20*	*31/2*

DATE	TIME	SINGLE WEIGHT VALUES										AVG	S.D.	CV%
28-09-2001	*08:35*											*131.0*	*2.1*	*1.60*
	09:05											*131.7*	*1.8*	*1.37*
	09:35											*132.2*	*1.7*	*1.29*
	10:05											*133.5*	*1.8*	*1.36*
	10:35											*132.9*	*1.6*	*1.20*
	11:05											*131.2*	*1.7*	*1.30*
	11:35											*131.8*	*1.2*	*0.91*
	12:05											*132.2*	*1.4*	*1.06*
	12:35											*132.9*	*1.5*	*1.13*
	13:05											*132.7*	*~~2~~ 0.9*	*0.68*
	13:35											*133.3*	*1.5*	*1.13*
	14:05											*132.8*	*1.6*	*1.2*
	14:35											*132.5*	*1.5*	*1.13*
	15:05											*132.3*	*1.8*	*1.36*
	15:35											*132.1*	*1.5*	*1.14*
01-10-2001	*08:35*											*132.6*	*2.0*	*1.51*
	09:01											*131.5*	*1.2*	*0.91*
	09:30	*132*	*134*	*134*	*131*	*131*	*131*	*133*	*133*	*130*	*130*	*131.8*	*1.3*	*1.00*
		132	*131*	*130*	*133*	*133*	*133*	*131*	*130*	*132*	*132*	*~~132.4~~*	[initials] *~~1.1~~*	*10 01* *~~0.83~~*
	10:00											*132.4*	*1.1*	*0.83*
	10:30											*132.1*	*0.9*	*0.72*
	11:00											*133*	*1.2*	*0.88*
	11:30											*133.3*	*1.3*	*0.95*
	12:00											*133.2*	*1.5*	*1.10*
	12:30											*133.2*	*1.3*	*0.96*
	13:00											*132.4*	*1.5*	*1.13*
	13:30											*134*	*1.3*	*0.98*
	14:00											*133.3*	*1.4*	*1.06*

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Pharmacia & Upjohn

Pharmaceutical Development / *Oral Solids and Warehousing*

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *31* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)

Scale model: *SARTORIUS* ID number: *SO - BL - 31*

Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations
Start/End of processing/day and every *30 min*	*131.50 mg*	*137.76 mg*	*125.24 mg*	*20*	*31/2*

DATE	TIME	SINGLE WEIGHT VALUES	AVG	S.D.	CV%
01-Oct.-01	*14:30*		*132.1*	*1.4*	*1.07*
	15:00		*132.6*	*1.3*	*0.99*
	15:30		*131.7*	*1.3*	*1.02*
	16:00	*MACHINE STOP* [initials]			
	16:20		*131.5*	*1.5*	*1.14*
	16:50		*133*	*1.5*	*1.14*
02-10-01	*08:20*		*130.6*	*1.8*	*1.41*
	08:50		*130.5*	*1.6*	*1.23*
	09:20		*131.6*	*1.9*	*1.42*
	09:50		*131.9*	*1.6*	*1.23*
	10:10	*Machine Stop* [initials]			
	10:40		*133*	*1.0*	*0.75*
	11:10		*131.5*	*1.8*	*1.36*
END	*11:40*		*130.9*	*1.2*	*0.94*
		[initials]			

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Pharmacia & Upjohn

Pharmaceutical Development / *Oral Solids and Warehousing*

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72/69*	Page: *32* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)

EQUIPMENT: *SOTAX DT 3* ID number: *SO - DG - 01*

FREQUENCY	LIMITS	IMMERSION FLUID	No. controls per inspection	No. OPERATIONS
Start/End of processing/day and every *4 hours*	≤ *30* min	*TDI H2O*	*6*	*31/3*

DATE	TIME	CONTROLS ON IMMERSION FLUID	SINGLE VALUES					
20 Sept. 01	*16:00*	Temp: *37* °C Level: *Conforms*	*6'00"*	*6'30"*	*6'59"*	*7'00*	*2'30"*	*7'50"*
20 Sept. 01	*12:00*	Temp: *37.5* °C Level: *Conforms*	*3"*	*3'20"*	*3'30"*	*7'40"*	*3'50"*	*4'10"*
21 Sept. 01	*9:30*	Temp: *37.5* °C Level: *Conforms*	*4'18"*	*5'00"*	*5'30"*	*6'00*	*6'30"*	*7'40"*
21 Sept. 01	*12:00*	Temp: *37.5* °C Level: *Conforms*	*4'50"*	*5'10"*	*5'30"*	*5'40"*	*6'20"*	*7'30"*
24 Sept. 01	*09:10*	Temp: *37.5* °C Level: *Conforms*	*5'30"*	*5'50"*	*6'10"*	*6'50"*	*7'30"*	*8'00"*
24 Sept. 01	*13:10*	Temp: *37.4* °C Level: *Conforms*	*4'00"*	*5'50"*	*6'30"*	*7'10"*	*7'30"*	*7'50"*
24-Sept. 01	*16:30*	Temp: *37.4* °C Level: *Conforms*	*5'00"*	*6'20"*	*6'40"*	*6'50"*	*3'00"*	*7'10"*
25-09-01	*9:30*	Temp: *37.5* °C Level: *Conforms*	*4'25"*	*5'00"*	*5'15"*	[illegible] ~~*6'50"*~~ *6'50"*	*6'55"*	*7'20"*
25-09-01	*13:35*	Temp: *37.4* °C Level: *Conforms*	*5'10"*	*5'50"*	*6'10"*	*6'25"*	*7'00"*	*7'35"*
25-09-01 [illegible] ~~*26-09-01*~~ *STOP*	*14:30* ~~*15:15*~~ [illegible]	Temp: *37.5* °C Level: *Conforms*	*4'55"*	*5'10"*	*5'15"*	*6'15"*	*6'50"*	*7'10"*
26-09-01 **SEE NOTE*	*10:16*	Temp: *37.5* °C Level: *Conforms*	*5'25"*	*5'45"*	*6'25"*	*6'50"*	*7'10"*	*7'20"*
27 Sept. 01	*08:30*	Temp: *37.4* °C Level: *Conforms*	*5'10"*	*5'50"*	*6'10"*	*6'50"*	*7'20"*	*7'50"*

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72-69*	Page: *33* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)

EQUIPMENT: *SOTAX DT 3* ID number: *SO-DG-01*

FREQUENCY	LIMITS	IMMERSION FLUID	No. controls per inspection	No. OPERATIONS
Start/End of processing/day and every *4 hours*	≤ *30* min	*TDI H2O*	*6*	*31/3*

DATE	TIME	CONTROLS ON IMMERSION FLUID	SINGLE VALUES					
22 Sept. 01	*12:30*	Temp: *37.4* °C Level: *Conforms*	*6'00"*	*6'50"*	*7'10"*	*8'00*	*8'30"*	*8'50"*
22 Sept. 01	*16:45*	Temp: *37.4* °C Level: *Conforms*	*5'50"*	*6'20"*	*6'50"*	*7'00*	*7'20"*	*7'40"*
28/09/01	*8:30*	Temp: *36.8* °C Level: *Conforms*	*7'30"*	*8'30"*	*9'10*	*9'30*	*'935*	*9'40*
28/Sept/01	*12:30*	Temp: *37.2* °C Level: *Conforms*	*6'50"*	*7'20*	*7'40"*	*7'50"*	*8'00"*	*8'30"*
28/Sept/01	*15:35*	Temp: *37.4* °C Level: *Conforms*	*7'00"*	*7'20"*	*3'50"*	*8'10"*	*8'40"*	*9'00"*
01/Oct./01	*08:45*	Temp: *37.4* °C Level: *Conforms*	*5'10"*	*5'30"*	*5'50"*	*6'20"*	*7'30"*	*7'50"*
01/Oct./01	*12:45*	Temp: *37.4* °C Level: *Conforms*	*6'40"*	*6'50"*	*7'10*	*7'30"*	*7'50"*	*8'10"*
01/Oct./01	*16:50*	Temp: *37* °C Level: *Conforms*	*6'10"*	*7'50"*	*8'30"*	*8'50"*	*9'00"*	*9'20"*
02/10/01	*8:40*	Temp: *36.8* °C Level: *Conforms*	*6'30"*	*6'45"*	*7'30"*	*8'05"*	*8'45"*	*10'30"* *CPS that floats* [initials] *2/10/01*
02/Oct./01	*11:40*	Temp: *37.2* °C Level: *Conforms*	*7'00"*	*7'20"*	*7'50"*	*8'00"*	*8'15"*	*9'20"*
		Temp: ____ °C Level: ____			[initials]			
		Temp: ____ °C Level: ____						

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room:	Page: *34* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)

EQUIPMENT: _____ ID number: _____

FREQUENCY	LIMITS	IMMERSION FLUID	No. controls per inspection	No. OPERATIONS
Start/End of processing/day and every *4 hours*	≤ *30* min	*TDI H_2O*	*6*	*31/3*

DATE	TIME	CONTROLS ON IMMERSION FLUID	SINGLE VALUES					
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____	[initials] *5/10/01*					
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						
		Temp: _____ °C Level: _____						

OPERATOR'S SIGNATURE: .....

VERIFIER'S SIGNATURE: .....

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: .....

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *72*	Page: *35* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		**DISTRIBUTION into CAPSULES**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
2 Oct. 01	*32*	**END OF DISTRIBUTION**	Date: *02-04-01* Time: *11:40*	[signature]	[signature]
02-03 Oct 01	*33*	**Controls on the finished product**		[signature]	[signature]
	33/1	Using the capsules sampled in point *29*, prepare and carry out the following samples:			
	33/2	No.: *106* for section controls	No.: *106*		
	33/3	No.: *50* for chemical controls	No.: *50*		
	33/4	No.: *30* for dissolution and possible technological controls by SF/Pharmaceutical Controls	No.: *30*		
	33/5	No.: *310* for bacterial loads *(40g)*	No.: *310* *(40g)*		
	33/6	No.: – for –	No.: –		
02-03 Oct 01	*34*	**Section technological controls**		[signature]	[signature]
	34/1	Perform the following section controls and report the data on the appropriate section regarding the FINISHED PRODUCT ☒ DURING PROCESSING ☐	Data reported on: FINISHED PRODUCT ☒ DURING PROCESSING ☐		
	34/2	Uniformity of weight/average weight (SOP SF.CI 051)	☒		
	34/3	Disintegration (SOP SF.CI 015)	☒		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: *72/69* *53* Page: *36* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base) **DISTRIBUTION into CAPSULES**

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
				[initials]	[initials]
	35	**Analytical controls on the finished product**			
07 Oct. 01	*35/1*	Send the above taken samples for the execution of the following controls and fill in the appropriate section regarding the: IN PROCESS ANALYTIC CONTROLS ☐ SENDING FOR FINISHED PRODUCT ANALYSIS ☒	Data reported on: IN PROCESS ANALYTIC CONTROLS ☐ SENDING FOR FINISHED PRODUCT ANALYSIS ☒		
	35/2	Titer ☒	☒		
	35/3	Correlated substances ☒	☒		
	35/4	Uniformity of content ☒	☒		
	35/5	Karl Fisher ☒	☒		
	35/6	Uniformity of weight ☒	☒		
	35/7	Dissolution ☒	☒		
	35/8	Bacterial load ☒	☒		
	35/9	Other: *IDENTIFICATION* ☒	☒		
3-10-01	*36-*	**Metal detector control**	*OPERATIONS PERFORMED ROOM 53*		
	36/1	At the end of the distribution, pass the suitable capsules through the metal detector	Model: *PRISMA* ID number: *SO/AT/02* Cleaning verification: *O.K.* Operative parameters: *SENSITIVITY PROGRAM*	[signature]	[signature]
	36/2	Verify the number of capsules discarded at the end of the operation	Discarded capsules: Gross: .....g Tare: .....g Net: .....g Equal to ..... (number) capsules as calculated based on the average weight	[signature]	[signature]
4-10-01	*36/3-*	Take care to send the discarded capsules to be destroyed.	☒		

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: 37 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

IN PROCESS ANALYTICAL CONTROLS

OPER. No.	DATE	SAMPLE No.	Numeric or ponderal quantity	CONTROL TYPE	LABORATORY	RESPONSE No. and DATE	OPERATOR	VERIFIER
3/1	*17.09. 01*	*1*	*150 ul*	*BACTERIAL LOAD CONTRAST H_2O 42*	*microbiological* [illegible]	*200071017 25/09/01*	[initials]	[initials]
25/5	*19-09-01*	*10*	*2g*	*MIX HOMOGENEITY*	*AD5*	*20012723 24/09/01*	[initials]	[initials]

TO SEND TO FINISHED PRODUCT ANALYSIS

DATE	Numeric or ponderal quantity	CONTROL TYPE	LABORATORY	RESPONSE No. and DATE	OPERATOR	VERIFIER
03-Oct-01	*50* [initials]	*CHEMICAL CONTROLS*	*ANALYTICAL ADS*	*20013158 13/11/01*	[initials]	[initials]
03-Oct-01	*30* [initials]	*DISSOLUTION AND EV.*	*ANALYTICAL ADS*	*20013158 13/11/01*		
07-Oct-01	*310* [initials]	*BACTERIAL LOAD*	*BIOLAB* [initials] *10.10.01* ~~*ANALYTICAL ADS*~~	*20013158 13/11/01*		

Checked by:_____

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: *38* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

TECHNOLOGICAL CONTROLS ON THE FINISHED PRODUCT

DATE	CONTROL	LIMITS/REFERENCES	RESULT	OPERATOR	VERIFIER
02-Oct 01	**WEIGHT** **SOP SF.CI 051**	Theoretical: *131.50* mg Minimum: *137.76* mg Maximum: *125.24* mg	Scale model: *SARTORIUS* ID number: *SO / BL / 31* *SEE ATTACHMENT* [initials]	[initials]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: *39* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

TECHNOLOGICAL CONTROLS ON THE FINISHED PRODUCT

DATE	CONTROL	LIMITS/REFERENCES	RESULT	OPERATOR	VERIFIER
02-Oct 01	**AVERAGE WEIGHT** **SOP SF.CI 048**	Theoretical: *131.50* mg Minimum: *128.37* mg Maximum: *136.63* mg	Average: *132.3* mg S.D.: *1.2* C.V.%: *1.31*	[initials]	[initials]
02-Oct 01	**DISINTEGRATION** **SOP SF.CI 015**	Limit: *<30'* Immersion fluid: *WATER 7D1 37°C* Disks: Yes ☐ No ☒	Disintegrator: *SOTAX DT3* ID No.: *SO / DG / 01* Immersion fluid: *TDI H_2O* Temperature: *37.4* °C Liquid level: *Conforms* Disks: Yes ☐ No ☒ *6'50"* *7'20"* *7'50"* *8'10"* *8'30"* *8'55"*	[initials]	[initials]
	LOSS OF WEIGHT **SOP SF.CI 029**	Limit: _____ Temperature: _____ °C Time: _____ _____	Equipment: _____ _____ ID No.: ____/____/____ Temperature: _____ °C Time: _____ minutes Loss of weight: _____ %		
	FRIABILITY **SOP SF.CI 025**	Quantity for the control: _____	Friabilimeter: _____ ID No.: ____/____/____ [initials] 13-9 2001 Initial weight: _____ g Final weight: _____ g Friability: _____ %		

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Room: 53 Page: ~~39~~ of 45

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

DISTRIBUTION into CAPSULES

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
3-10-2001	37	**Processing yield controls**			
	37/1-	At the end of the processing collect the capsules and place them in the following primary packaging: *DOUBLE PE BAG / KRAFT BARREL*	Primary packaging used: *DOUBLE PE BAG /* *KRAFT BARREL* [initials] *4-10-01*	[signature]	[signature]
	37/2	Determine the quantity of product obtained in ponderal terms.	Ponderal yield: *BARREL 1* / *BARREL 2* / *BARREL 3* Gross: *10.00 kg* / *11344* g *13845* Tare: *2.850 kg* / *3003* g *2838* Net: *7.150 kg* / *8341* g(H) *8-2-08* [initials] *4-10-01*		
	37/3		*NOTE: The weighing will be performed direct at the end of the sorting, and parallel-channeled into the capsule sealing phase.* [initials] [illegible]		
~~4-10-2001~~ [initials]	37/4	Calculate the numeric quantity of the obtained product: Numeric yield = H / average weight(*)	Numeric yield: *~~16549~~* = No _____ (G) [initials] *04/10/01*	[signature]	[signature]
	37/5	(*) Obtained by final controls End of processing yield: (G / THEORETICAL(*)) * 100 (*) T from page 1 *(140000 qs)*	% Yield: _____ = _____ % *The final yield is calculated after the sorting.* [initials] *04/10/01*		
04-10 2001	38	Calculate the mix quantity and residual shells and see to: SENDING THE MIX AND SHELLS TO BE DESTROYED ☒ SET ASIDE THE MIX ☐ NOTE:_____	Residual mix: Gross: *260* g, Tare: *20* g, Net: *240* g Residual shells: Gross: *600* g, Tare: *120* g, Net: *480* g SENT TO BE DESTROYED ☒ SET ASIDE ☐	[signature]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: *41* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01/10/01 *1-4-10-01*	*39* *39/1*	**Sorting the lot** [initials] [illegible]*/10/01* Proceed to the sorting of the sample as described in the following section. At the end of processing, collect a number of samples equal to 3% of the numeric yield of the lots at the end of processing, from various points in the bulk. Report the results on the corresponding page. *IN ORDER TO ELIMINATE THE CAPSULES MARKED BY THE CAPSULE SEALER PROCEED WITH THE UNIT SORTING OF THE* [illegible] *SAMPLE CAPSULES WHICH HAVE BEEN PRODUCED AND DEPOWDERED. START THE PARALLEL SORTING IN THE FINAL SEALING PHASE.* *SEE NOTE.* [initials] *01/10/01*	Quantity sampled: No. /	[initials]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: *42* of *45*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

SORTING of the SAMPLES from the PRODUCT OBTAINED at the END OF PROCESSING

PHARMACEUTICAL FORM: **CAPSULE**

QUANTITY OBTAINED: No. .....(A)

QUANTITY to be SORTED: No. ..... (B) [Equal to 3% of A]

SORTING LIMITS – PRIMARY DEFECTS: NOT MORE than THREE UNITS

APPEARANCE: _____

	DATE	DATE	DATE	DATE	DATE	DATE
LIST OF PRIMARY DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
CAPSULES BROKEN ON THE TIPS						
CAPSULES BROKEN ON THE BODY						
BODY IS VISUALIZED ON THE HEAD						
TOTAL [initials]	*5/10/01*					
LIST OF SECONDARY DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
TOTAL						

NOTE: _____

Operator's signature	**Verifier's signature**	**Checked by:**

APPEARANCE CONFORMITY

LOT CONFORMS for APPEARANCE ☐

LOT DOES NOT CONFORM for APPEARANCE go to UNIT SORTING ☐

SECTION CHIEF SIGNATURE: _____

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: *54*	Attachment No.: *1* page *42*
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		

UNIT SORTING

SORT TYPE: MANUAL ☒ WITH A SORTER ☐

SORTER MODEL: .....

CLEANING VERIFICATION: .....

	DATE *1-10-2001*	DATE *2-10-01*	DATE *3-10-01*	DATE *4-10-01*	DATE	DATE
LIST OF DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
CAPSULES BROKEN ON THE TIPS						
CAPSULES BROKEN ON THE BODY						
BODY IS VISUALIZED ON THE HEAD	*75*	*220*	*36*	*0*		
CAPSULES CRUSHED AT TIPS						
CAPSULES WITH DOUBLE BODY OR DOUBLE HEAD	*10*	*35*	*2*	*0*		
					[initials] *4-10-01*	
PARTIAL TOTAL	*85*	*255*	*38*	*0*		

FINAL BALANCE

QUANTITY TO BE SORTED: ..... (K)

TOTAL SORTED OUT TO BE DISCARDED: ..*378* [initials]... (Y)

TOTAL SORTED INTO SELECTION: ..... (X) X= K-Y

NOTE: K = Processing end yield – sample sorted out to be discarded

THE WEIGHING, MADE IN PROCESS, WILL BE PERFORMED AT THE END OF THE SORTING WORK AND ARE TO BE VERIFIED BY A METAL DETECTOR. [initials] *01/10/2001*

NOTES: *On the 1st and 2nd of October capsules sorted from production with mealine with technical problems! The production root setting is correct and has been unit sorted despite the fact the capsules with anomalies or broken have now been diminished.* [initials] *2/10/2001*

Operator's signature: [signature]

Verifier's signature: [signature]

Edition No.: 7 of 10/05/99
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: *43* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 10 01	*39/2*	If the results of the sampling sorting are outside the set limits, proceed to unit sorting of the lot as described in the attached form. *NOTE: THE UNIT SORTING IS DIRECTLY DONE IN ORDER TO ELIMINATE THE DEFECTIVE CAPSULES (THOSE MARKED ON THE TOP) CAUSED BY TECHNICAL DIFFICULTIES WITH THE CAPSULE SEALER.* [initials] 01/10/01	☐		
	39/3	At the end of the sorting operation, send the discarded product to be destroyed.	☒	[signature]	[signature]
3-10-01	*40*	**Counter sampling**			
	40/1	Sample *100* (number) units and package them in: *PE BOTTLES*	Quantity sampled: No. *100* ☒ *SEE NOTE* [initials] *08/10/01*	[signature]	[initials]
4-10-01	*41*	**Final lot yield control**	*THE WEIGHTS HAVE BEEN PROVIDED HERE AS SUMS OF THOSE RELATIVE TO THE TWO PARTS* Available product *SEE NOTES (END SUM)*		
	41/1	Proceed to the quantitative verification of the available product.	Gross: *22390* g [initials] *4/10/2001* Tare: *5841* g Net: *16549* g (U)	[signature]	[initials]
	41/2	Numeric yield = U / average weight(*) (*) Taken from the final controls	Numeric yield = *125087* (V)		
	41/3	% Yield = (V / THEORETICAL(*)) * 100 (*) T of page 1	% Yield: *89.3* (Z)		
4-10-01	*42*	**Deposit in the warehouse**			
	42/3	Load the finished product and the counter sample into the SF/Warehouse, stocking them as: *T.A.*	☒	[signature]	[initials]

Product: SU 10398 (PNU-290940AD) Lot: I83G03 Page: *45* of *45*

Pharmaceutical form: Capsule Dosage: 25 mg (as a free base)

LOT APPROVAL

OPERATIVE VERIFICATION of the "ORAL SOLIDS" SECTION

NOTES: _____

SIGNATURE: [signature] DATE: *08/10/2001*

CHIEF of "ORAL SOLIDS and WAREHOUSING" APPROVAL

RESULTS: APPROVED ☒ REJECTED ☐

NOTES: _____

SIGNATURE: [signature] DATE: *13/11/2001*

USE AUTHORIZATION OF THE CHIEF of "Q.C./PHARMACEUTICAL CONTROLS"

RESULTS: APPROVED ☒ REJECTED ☐

NOTES: _____

SIGNATURE: [signature] DATE: *30/11/2001*